III. AMENDMENTS TO CLAIMS

Claims 4, 10, 18, 24, 30-33 and 38 are cancelled, without prejudice. Please add new claims 41-50 as set forth below.

IN THE CLAIMS:

1. *(~~Once~~**Currently** Amended)* A method for ~~determining whether~~**screening** an individual ~~is likely to have gastrointestinal~~**for colorectal** cancer, the method comprising determining ~~a parameter representing~~ the total concentration of TIMP-1 in a ~~body fluid~~**plasma** sample of said individual, ~~other than blood serum,~~ and indicating the individual as ~~having a high likelihood of having gastrointestinal~~**likely to have colorectal** cancer if the ~~parameter~~ **total concentration of TIMP-1** is ~~at or beyond a discriminating~~ higher than the total conc of TIMP-1 measured in healthy control population a value and indicating the individual as unlikely ~~of having gastrointestinal~~**to have colorectal** cancer if the ~~parameter~~ **total concentration of TIMP-1** is ~~not at or beyond the discriminating value, whereby the likelihood that said individual is likely to~~ lower than the total conc. of TIMP-1 **has or will** have ~~gastrointestinal~~**colorectal** cancer is determined, the discriminating value being a value which has been ~~determined by measuring said parameter~~ **the total concentration of TIMP-1** measured in both a healthy control population, ~~and a population with known gastrointestinal~~**colorectal** cancer, thereby determining said discriminating value which identifies the ~~gastrointestinal~~**colorectal** cancer population with ~~a predetermined specificity and/or~~ a predetermined sensitivity **or predetermined specificity.**

~~4. *(Once Amended)* A method according to claim 1, wherein the parameter determined is the value obtained by combining the concentration of total TIMP-1 with the concentration of free TIMP-1.~~

5. *(~~Original~~**Currently Amended**)* A method according to claim 4~~,~~ **41,** wherein the ~~combining~~ **combination** is performed by logistic regression analysis.

6. *(~~Original~~**Currently Amended**)* A method according to ~~any of the preceding~~ claims~~,~~ **1 or 5,** which comprises additionally determining at least one second parameter, the second parameter representing the concentration of an additional **tumour** marker different from any form of TIMP-1, in a body fluid sample from the individual.

7. *(~~Original~~**Currently Amended**)* A method according to claim 6, wherein the ~~first parameter representing the~~**total** concentration of TIMP-1 in ~~body fluid samples~~ **the plasma sample** and the ~~at least one second parameter~~**concentration of the additional tumour marker** different from any form of TIMP-1 are combined to result in a combined parameter and indicating the individual as ~~having a high likelihood of having~~**likely to have colorectal** cancer if the combined parameter is at or beyond a discriminating value and indicating the individual as unlikely ~~of having~~ **to have colorectal** cancer if the combined parameter is not at or beyond the discriminating value.

8. *(Original)* A method according to claim 7, wherein the combining is performed by logistic regression analysis.

9. *(~~Original~~**Currently Amended**)* A method according to claim 7 ~~or 8~~ , wherein the discriminating value of the combined parameter is a value which has been determined by determining said combined parameter in both a healthy control population and a population with known **colorectal** cancer, thereby determining the discriminating value which identifies the **colorectal** cancer population with a

predetermined specificity or a predetermined sensitivity.

~~10. *(Original)* A method according to any of claims 6-9, wherein the at least one second parameter determined is a parameter representing the concentration of a tumour marker.~~

11. *(~~Original~~**Currently Amended**)* A method according to claim ~~10,~~**9,** wherein the tumour ~~marked~~ **marker** is selected from the group consisting of CEA, soluble U-PAR, cathepsin B, HER2-neu, CA15-3 and YKL-40.

12. *(Original)* A method according to claim 11, wherein the at least one second parameter determined is the concentration of CEA.

13. *(~~Once~~**Currently** Amended)* A method according to claims 1, **41,** ~~4~~**42** or ~~5~~**5,** wherein the individual is a member of an unselected population.

14. *(~~Once~~**Currently** Amended)* A method according to claims 1, **41,** ~~4~~**42** or ~~5~~**5,** wherein the individual is a member of a population already identified as having an increased risk of developing cancer.

15. *(~~Once~~**Currently** Amended)* A method for ~~determining whether a patient~~**screening an individual,** who has been treated for primary breast cancer ~~is likely to have~~**, for** metastatic breast cancer, comprising determining ~~a parameter representing~~ the total concentration of TIMP-1 in a ~~body fluid~~**plasma** sample of said individual, ~~other than blood serum,~~ and indicating the individual as ~~having a high likelihood of having~~**likely to have** metastatic breast cancer if the ~~parameter~~ **total concentration of TIMP-1** is at or beyond a discriminating value and indicating the individual as unlikely ~~of~~**to** ~~having~~**have** metastatic breast cancer if the ~~parameter~~ **total concentration of TIMP-1**

is not at or beyond the discriminating value, whereby the likelihood that said individual ~~is likely to~~**has or will** have metastatic breast cancer is determined, the discriminating value being a value which has been determined by measuring ~~said parameter~~**the total concentration of TIMP-1** in both a healthy control population and a population with known metastatic breast cancer, thereby determining said discriminating value which identifies the metastatic breast cancer population with a predetermined ~~specificity and/or a predetermined~~ sensitivity **or a predetermined specificity**.

~~18. *(Once Amended)* A method according to claim 15, wherein the parameter determined is the value obtained by combining the concentration of total TIMP-1 with the concentration of free TIMP-1.~~

19. *(~~Original~~**Currently Amended**)* A method according to claim ~~18,~~ **42,** wherein the ~~combining~~**combination** is performed by logistic regression analysis.

20. *(~~Original~~**Currently Amended**)* A method according to ~~any of~~ claims 15-**or** 19, which comprises additionally determining at least one second parameter, the second parameter representing the concentration of an additional **tumour** marker different from any form of TIMP-1, in a body fluid sample from the individual.

21. *(~~Original~~**Currently Amended**)* A method according to claim 20, wherein the ~~first parameter representing the~~**total** concentration of TIMP-1 in ~~body fluid samples~~**the plasma sample** and the ~~at least one second parameter~~**concentration of the additional tumour marker** different from any form of TIMP-1 are combined to result in a combined parameter and indicating the individual as ~~having a high likelihood of having~~**likely to have** metastatic cancer if the combined parameter is at or beyond a

discriminating value and indicating the individual as unlikely ~~of~~**to** ~~having~~**have** metastatic cancer if the combined parameter is not at or beyond the discriminating value.

22. *(Original)* A method according to claim 21, wherein the combining is performed by logistic regression analysis.

23. *(Original)* A method according to claim 21 ~~or 22~~, wherein the discriminating value of the combined parameter is a value which has been determined by determining said combined parameter in both a healthy control population and a population with known metastatic cancer, thereby determining the discriminating value which identifies the metastatic cancer population with a predetermined specificity or a predetermined sensitivity.

~~24. *(Original)* A method according to any of claims 20-23, wherein the at least one second parameter determined is a parameter representing the concentration of a tumour marker.~~

25. *(~~Original~~**Currently Amended**)* A method according to claim ~~24,~~**20,** wherein the tumour ~~marked~~ **marker** is selected from the group consisting of CEA, soluble u-PAR, cathepsin B, HER2-neu, CA15-3 and YKL-40.

26. *(Original)* A method according to claim 25, wherein the at least one second parameter determined is the concentration of CEA.

27. *(~~Once~~**Currently** Amended)* A method according to claim 15, wherein the determination is performed at several time points at intervals as part of a monitoring of a cancer patient after the treatment for primary **breast** cancer.

28. *(~~Once~~**Currently** Amended)* A method according to claim 1, ~~used for detecting~~**which detects** early stage cancer.

29. *(Original)* A method according to claim 28, wherein the early stage cancer is selected from the group consisting of colon cancer Dukes' stage A, colon cancer Dukes' stage B, colon cancer Dukes' stage C, rectal cancer Dukes' stage A, rectal cancer Dukes' stage B and rectal cancer Dukes' stage C.

~~30. *(Once Amended)* A method according to claims 1 or 15, wherein the body fluid is selected from the group consisting of blood (plasma), faeces, urine and cerebrospinal fluid.~~

~~31. *(Original)* A method according to claim 30, wherein the body fluid is plasma.~~

~~32. *(Original)* A method according to claim 30, wherein the body fluid is blood.~~

~~33. *(Original)* A method according to claim 30, wherein the body fluid is urine.~~

34. *(~~Once~~**Currently** Amended)* A method according to claims 1 or 15, wherein the total concentration ~~determination~~ of TIMP-1 is performed by means of an immuno assay or an activity assay.

35. *(Original)* A method according to claim 34, wherein the immuno assay is an ELISA.

36. *(Original)* A method according to claim 34, wherein the activity assay is

zymography.

~~37. *(Original)* A method according to any of the preceding claims, wherein the cancer type is selected from the group consisting of colon cancer, rectal cancer and metastatic breast cancer, lung cancer, prostate cancer, ovarian cancer, cervical cancer, liver cancer and gastric cancer.~~

~~38. *(New)* A method according to claim 1 wherein the gastrointestinal cancer is colorectal cancer.~~

39. *(~~New~~**Currently Amended**)* A method according to claim 1 wherein the ~~gastrointestinal~~ **colorectal** cancer is colon cancer.

40. *(~~New~~**Currently Amended**)* A method according to claim 1 wherein the ~~gastrointestinal~~**colorectal** cancer is rectal cancer.

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~~41. *(New)* A method for screening an individual for colorectal cancer, the method comprising determining the combination of the concentration of total TIMP-1 with the concentration of free TIMP-1 in a plasma sample of said individual, and indicating the individual as likely to have colorectal cancer if the combination of the concentration of total TIMP-1 with the concentration of free TIMP-1 is at or beyond a discriminating value and indicating the individual as unlikely to have colorectal cancer if the combination of the concentration of total TIMP-1 with the concentration of free TIMP-1 is not at or beyond the discriminating value, whereby the likelihood that said individual has or will have colorectal cancer is determined, the discriminating value being a value which has been determined by measuring the combination of the~~

concentration of total TIMP-1 with the concentration of free TIMP-1 in both a healthy control population and a population with known colorectal cancer, thereby determining said discriminating value which identifies the colorectal cancer population with a predetermined sensitivity or a predetermined specificity.

42. *(New)* A method for screening an individual, who has been treated for primary breast cancer, for metastatic breast cancer, the method comprising determining the combination of the concentration of total TIMP-1 with the concentration of free TIMP-1 in a plasma sample of said individual, and indicating the individual as likely to have metastatic breast cancer if the combination of the concentration of total TIMP-1 with the concentration of free TIMP-1 is at or beyond a discriminating value and indicating the individual as unlikely to have metastatic breast cancer if the combination of the concentration of total TIMP-1 with the concentration of free TIMP-1 is not at or beyond the discriminating value, whereby the likelihood that said individual has or will have metastatic breast cancer is determined, the discriminating value being a value which has been determined by measuring the combination of the concentration of total TIMP-1 with the concentration of free TIMP-1 in both a healthy control population and a population with known metastatic breast cancer, thereby determining said discriminating value which identifies the metastatic breast cancer population with a predetermined sensitivity or a predetermined specificity.

43. *(New)* A method according to claim 6, wherein the additional tumour marker is a colorectal tumour marker.

44. *(New)* A method according to claim 43, wherein the total concentration of TIMP-1 in the plasma sample and the concentration of the additional tumour marker

different from any form of TIMP-1 are combined to result in a combined parameter and indicating the individual as likely to have colorectal cancer if the combined parameter is at or beyond a discriminating value and indicating the individual as unlikely to have colorectal cancer if the combined parameter is not at or beyond the discriminating value.

45. (New) A method according to claim 44, wherein the combining is performed by logistic regression analysis.

46. *(New)* A method according to claim 44, wherein the discriminating value of the combined parameter is a value which has been determined by determining said combined parameter in both a healthy control population and a population with known colorectal cancer, thereby determining the discriminating value which identifies the colorectal cancer population with a predetermined specificity or a predetermined sensitivity.

47. *(New)* A method according to claim 46, wherein the tumour marker is selected from the group consisting of CEA, soluble U-PAR, cathepsin B, HER2-neu, CA15-3 and YKL-40.

48. *(New)* A method according to claim 47, wherein the at least one second parameter determined is the concentration of CEA.

49. *(New)* A method according to claim 43, wherein the individual is a member of an unselected population.

50. *(New)* A method according to claim 43, wherein the individual is a member of a population already identified as having an increased risk of developing cancer.